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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/489,667	01/19/2000	Stephen Donovan	D-2875	6119

7590 03/31/2006

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 03/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/489,667	DONOVAN, STEPHEN	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69,71-73 and 75-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *69,71-73 and 75-76* is/are allowed.

6)☒ Claim(s) *77-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 69, 71-73 and 75-80 are pending.

Applicants' amendment filed January 24, 2006 is acknowledged. Applicants' response has been fully considered. Claims 69, 71-73 and 75-76 have been amended, and claims 70 and 74 have been cancelled. Therefore, claims 69, 71-73 and 75-80 are examined. In view of applicants' amendment and arguments, the potential interference of instant application with U. S. patent 6,632,440 is dismissed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 77-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent for treating pain comprising a modified botulinum neurotoxin comprising a light chain (L-chain) or L-chain fragment of a botulinum neurotoxin containing the active proteolytic enzyme domain, a botulinum neurotoxin H_N as the translocating domain, and no functional H_C domain wherein the modified botulinum neurotoxin is covalently coupled to Substance P, does not reasonably provide enablement for an agent for treating pain comprising a botulinum neurotoxin without a functional H_C domain covalently coupled to Substance P, wherein the domain structure of botulinum neurotoxin is not identified. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 77-80 encompass an agent for treating pain comprising a botulinum neurotoxin without a functional H_C domain covalently coupled to Substance P. The specification, however, only discloses cursory conclusions (pages 15-16) without data supporting the findings, which states that the present invention provides agents for treating pain comprising a clostridial neurotoxin (e.g., botulinum neurotoxin) or component thereof coupled to a targeting moiety such as Substance P, e.g., the H_C has been removed from the neurotoxin; L chain or a functional fragment of L-chain coupled to the targeting moiety; or the H_N domain, the L-chain and the targeting domain covalently coupled together. There are no indicia that the present application enables the full scope in view of the modified botulinum neurotoxin used for treating pain as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is encompassed. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the modified botulinum neurotoxins containing various domains which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification describes the preparation of chimeric LH_N (Example 1); and the use of LH_N-substance P in the treatment of various types of pain (Examples 2-8). However, there are no working examples indicating the claimed agents associated with variants except for LH_N-substance P.

(3). The state of the prior art and relative skill of those in the art:

The related art (e.g., Foster *et al.*, U.S Patent 5,989,545) teaches conjugating clostridial neurotoxins to targeting moieties in order to direct the inhibitory effect of clostridial neurotoxins toward primary sensory afferent neurons. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identification and use of the agents containing various domains of botulinum neurotoxins in the treatment of pain to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass an agent for treating pain comprising a botulinum neurotoxin without a functional H_C domain covalently coupled to Substance P, however, the effects of the agents containing a botulinum neurotoxin having various domain structures (e.g., the conjugate of L-chain or its fragment with substance P) are not sufficiently described in the specification, the invention is highly unpredictable regarding the structure of the active agent and its effect in the treatment of pain.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to an agent for treating pain comprising a botulinum neurotoxin without a functional H_C domain covalently coupled to Substance P. The specification has

demonstrated the use of LH_N-substance P in the treatment of various types of pain (Examples 2-8), however, it has not demonstrated the use of agents containing various domains of botulinum neurotoxins in treating pain, and there are no working examples indicating the claimed agents associated with variants except for LH_N-substance P. Furthermore, the specification has not shown the effects of agents containing various domains of botulinum neurotoxins in treating pain. Since the specification fails to provide sufficient guidance on the use of agents containing various domains of botulinum neurotoxins in treating pain, it is necessary to carry out undue experimentation to identify the active agents containing various domains.

(6). Nature of the Invention

The scope of the claims includes an agent for treating pain comprising a botulinum neurotoxin without a functional H_C domain covalently coupled to Substance P, but the specification has not shown the effect of the agents comprising various L-chain fragments and translocating domains of botulinum neurotoxins covalently coupled to substance P. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed variants, and the teachings in the specification are limited, therefore, it is necessary to carry out undue experimentation to identify the active agents and to assess its effect in the treatment of pain.

Conclusion

3. Claims 77-80 are rejected, and claims 69, 71-73 and 75-76 are free of art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
March 24, 2006